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LETTERS AND CORRESPONDENCE

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Uncommon Cause of Severe Pancytopenia: Toxoplasmosis

To the Editor: We describe a patient with a diagnosis of toxoplasmosis in whom all data are consistent with aplastic anemia. He was 21 years old and admitted to hospital for evaluation of a 3-week history of fever of unknown origin, epistaxis, fatigue, dizziness, and purpuric lesions. His initial laboratory examination revealed a hemoglobin of 10.4 g/dl, a hematocrit of 30.9%, and a corrected reticulocyte count of 0.2% with normochromic and normocytic indexes; white blood cell count was 2,400 cells/μl with 91% lymphoid cells, and platelets were 4,000 cells/μl. Bone-marrow examination revealed fatty replacement hypocellularity with a decrease of all hematopoietic precursors and a slight increase of plasma cells. Bone-marrow biopsy confirmed severe hypocellularity and fatty replacement, and was reported as consistent with aplastic anemia. His initial serologic examination revealed a toxoplasmosis serum IgG titer of 16 IU/ml and serum IgM titer of 13.45 IU/ml (normal values <8 IU/ml for IgG, and <0.55 IU/ml for IgM) (VIDAS Toxo IgG (TMX) and VIDAS Toxo IgM (TMX) bioMerieux Sa, France). The patient received no antiparasitic treatment in this period because of his immunocompetent condition. One month later the patient's laboratory values revealed a hemoglobin of 11.7 g/dl and a hematocrit of 32.7%, a white blood cell count of 4200 cells/μl with a normal differential, and platelets of 247.000 cells/μl. At the same time, his serologic examination showed an anti-toxoplasmosis serum IgG titer of >300 IU/ml and serum IgM titer of <2.42 IU/ml.

Pancytopenia with aplastic or hypoplastic marrow has been reported with increasing frequency in association with a variety of viral illnesses, especially viral hepatitis [1]. Rubella virus, Epstein-Barr virus, parvovirus, and several varieties of hemorrhagic virus infections are also known to cause selective depression of hemopoietic elements or pancytopenia. Pancytopenia has been reported occasionally in association with tuberculosis, and other mycobacterial infections, such as *M. kansassii, Brucellosis,* and sarcoidosis are common causes of pancytopenia in endemic areas [2]. Some authors have reported thrombocytopenia in association with toxoplasmosis [3]. Soulier-Lauper et al. [4] described a patient with pancytopenia, who had acute myeloid leukemia and underwent bone-marrow transplantation, of whom toxoplasma cysts were shown in the bone-marrow smears [4].

In our patient, initial and subsequent laboratory findings revealed positive serology for *Toxoplasma gondii* in the blood. One month later, toxoplasma serum IgG antibody titer was higher than IgM antibody titer with respect to initial levels, and all hematological parameters improved without any treatment except for supportive therapy.

The use of serologic tests for demonstration of specific antibodies to toxoplasma is the primary method of diagnosis, but the serologic markers need good clinical evaluation and comment [5]. The problem in serologic diagnosis is the high prevalence of IgG-class antibodies to toxoplasma in most populations. These antibodies reach peak concentration in 1–2 months after infection, and remain at high titers for many years. IgM-specific antibodies can be detected 2 weeks after infection, reach their peak concentration in 1 month, decline subsequently, and become undetectable usually within 6 months.

This case suggests that toxoplasmosis should be considered in the differential diagnosis of infectious causes of pancytopenia.

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Isolated Choroidal Leukemic Infiltration During Complete Remission

To the Editor: Ocular granulocytic sarcoma in AML patients during complete remission is very rare [1,2]. This report documents an AML patient with choroidal infiltration of leukemia cells during complete remission. The role of ocular hemorrhage that contains leukemia cells during active disease is discussed as a predisposing factor for latent seeding of leukemia cells into the choroid.

A 17-year-old woman was admitted with a rapidly progressive visual disturbance in November 1991. She was found to have bilateral retinal hemorrhages and abnormalities on hematologic examination. Bone marrow aspirate revealed a monotonous proliferation of peroxidase-positive blasts (72.8%) with distinct nucleoli and Auer rods. Surface marker analysis of

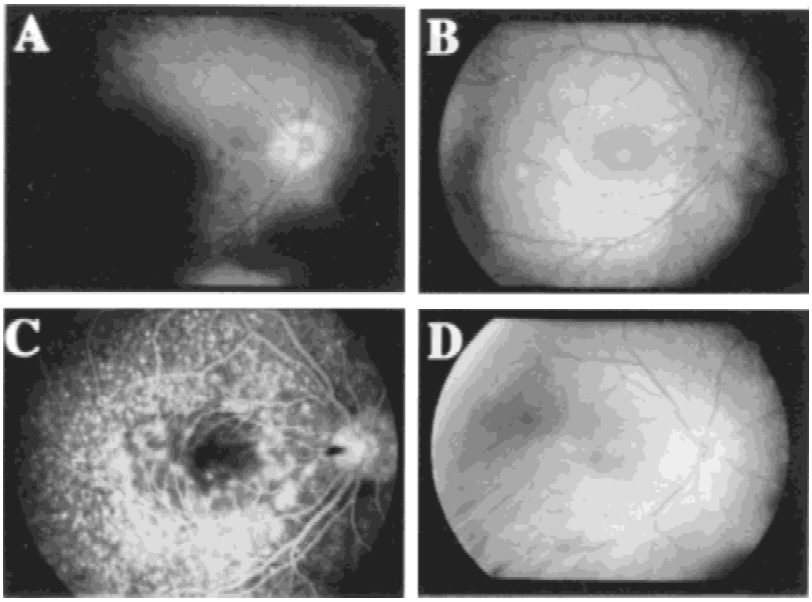

Fig. 1. Ophthalmoscopic findings of the right fundus. A: Blot retinal hemorrhages at first visit. B: Infiltration of leukemia cells into the choroid and resultant serous retinal detachment (before radiation therapy). C: Fluorescein angiography of right fundus before radiation therapy. Myriad diffuse leakage of dye was seen. D: Improvement of choroidal infiltration (after radiation therapy).

the blasts demonstrated: CD13(+), CD33(+), CD34(+), CD7(−), CD10(−), CD14(−), CD19(−). Chromosomal analysis of bone marrow leukemia cells showed karyotype abnormality: t(8;21) and loss of sex chromosome: −X. Therefore, she was finally diagnosed as AML-M2 according to the criteria of the French-American-British Cooperative Group classification (FAB), complicated by retinal hemorrhage. She attained a complete remission and all treatments were finished in October 1992. In September 1994, she suddenly presented a visual disturbance of the right eye. Ophthalmologic examination revealed choroidal infiltration of leukemia cells and infiltration-induced serous retinal detachment in the right eye. There was no evidence of CNS leukemia. Local radiation therapy improved her ophthalmologic findings (Fig. 1) and completely resolved her visual disturbance after receiving 30 Gy at the end of December 1994. In November 1994, we could not detect leukemia cells in the bone marrow using fluorescence *in situ* hybridization (FISH). Moreover, no leukemia cells in the bone marrow were detected by morphological examination and Southern blot analysis using the *AML1* probe in April 1995. She was last seen in complete remission in July 1995. However, she finally had bone marrow relapse in September 1995.

Although there was no histopathologic evidence for the direct infiltration of leukemia cells into the choroid, the visual disturbance in our patient was probably caused by choroidal infiltration of leukemia cells, given the ophthalmologic findings and the rapid therapeutic response to the local irradiation alone. So, we hypothesized that the initial retinal hemorrhage allowed ocular seeding of leukemia cells that became apparent 2 years after remission induction. Since frequency of ocular involvement in AML patients with retinal hemorrhage has not been reported, we could not conclude that there was a close relation between ocular involvement of AML and a history of retinal hemorrhage. Because there have been 13 (8.5%) cases of orbital involvement in 154 primary (or isolated) extramedullary leukemias [3], it may be necessary to irradiate for ocular prophylaxis in AML patients with a history of retinal hemorrhage during active disease in spite of organ toxicity of ocular irradiation.

In conclusion, local irradiation of ocular prophylaxis might be considered in AML patients, especially FAB-M2 and M4 subtypes [4], with retinal hemorrhage that contains leukemic cells. Frequency of ocular infiltration in patients with AML complicated by retinal hemorrhage and the efficacy of local irradiation for ocular prophylaxis in these patients must be studied.

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Therapy-Related Acute Myeloid Leukemia With Minimal Myeloid Differentiation (AML-M0) Associated With a t(11;19)(q23;p13.3) Translocation

To the Editor: Chromosomal translocations affecting band 11q23 and the *MLL* gene rearrangement are strongly associated with therapy-related acute myeloid leukemia (t-AML) after treatment with epipodophyllotoxin. Most cases of epipodophyllotoxin-induced t-AML are classified as FAB subtype